



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,134	07/02/2002	Raghuveer Basude	DRE-0063	8214
26259	7590	03/02/2006	EXAMINER	
LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			EBRAHIM, NABILA G	
			ART UNIT	PAPER NUMBER
			1618	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/980,134	Applicant(s) BASUDE ET AL.	
	Examiner Nabila G. Ebrahim	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/9/05 has been entered.

Status of claims

Claims 1-14 are pending in the application

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 and 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Rasor et al. US 5141738 (hereinafter "Rasor").

Rasor discloses a composition for ultrasound imaging comprising a microparticle having a hydrophobic surface (col. 8, lines 24-26) and a gas microbubble, (col. 6, lines 3-11). The gas microbubble attaches or in contact with the microparticle, (column 6, line 57). The compositions are prepared by methods including storing the microparticle in a gaseous environment and introducing the microparticles into a liquid, (col. 9 bridging to

Art Unit: 1618

10 and examples). Also, since the microparticle contains a lipophilic surface, it would have affinity for lipophilic gases such as perfluorocarbons that are somewhat lipophilic by nature. In addition, the step of forming the gas microbubble recited in claim 1 and 2 of the current application is considered a product by process limitation, wherein only a specific single step excludes adding surfactant, this limitation does not exclude surfactant in the microbubble and consequently does not differentiate over the prior art. Rasor also teaches that the ultrasonic diagnostics comprising a liquid vehicle containing (a) suspended therein microparticles of a mixture of at least one $C_8 - C_{20}$ fatty acid and at least one solid that is not a surfactant and (b) microbubbles (abstract), the disclosure does not include the surfactant and is administered intravenously (into the blood).

Claims 1-7 and 9-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Schneider US 5,271,928 (hereinafter "Schneider").

Schneider discloses a composition for ultrasound imaging comprising a microparticle having a hydrophobic surface (such as, a liposome) and microbubbles which are associated therewith, in that the liposomes stabilize the microbubbles, see (col. 4, lines 6-36). The compositions are prepared by a method of storing the liposomes in a gaseous environment and introducing the liposomes into a liquid, (col. 4, lines 37-55). The compositions may further include drugs, such as radionuclide for nuclear medicine, (col. 10, lines 3-5) as well as, a targeting moiety, (column 9, lines 36-66). Also, since the microparticle contains a lipophilic surface, it would have affinity for lipophilic gases such as perfluorocarbons that are somewhat lipophilic by nature. Schneider also disclosed that his composition is suitable for injection into the

bloodstream and body cavities of living beings, comprising a suspension of stabilized air or gas microbubbles in a physiologically acceptable aqueous carrier (claim 1).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rasor 5141738 or Schneider US 5271928 in view of Unger US 5542935 (hereinafter “Unger”).

Rasor and Schneider disclose compositions comprising a microparticle and microbubble for methods of ultrasound and/or drug delivery, as discussed above.

Rasor and Schneider fail to disclose that the methods of drug delivery include a step of insonating the desired site in the patient to rupture the microbubble thereby releasing a drug.

Unger discloses compositions comprising microbubbles that are useful for both ultrasound imaging and drug delivery, see abstract and column 35, lines 4-5. Unger teaches that the microbubbles may further comprise various drugs that are released by insonation to provide the advantage of site-specific delivery to a desired site, (e.g., the drug is not released until the particles reach the treatment site), (col. 35, lines 29+).

It would have been obvious to one of ordinary skill in the art to use the compositions disclosed by Rasor or Schneider for drug delivery by insonating the microbubbles at a desired site in vivo because Unger teaches that analogous gas-filled microbubbles may further contain various drugs to yield a drug delivery means having the advantage of site-specific delivery by insonating the microbubbles at a desired site in vivo. One of ordinary skill in the art would have been motivated to employ the drug delivery methods disclosed by Unger using the compositions disclosed by Rasor and Schneider to obtain a composition which is useful for both ultrasound imaging and site-specific therapy using a single administration, wherein the insonating step provides release of the drug specifically at the treatment site.

Response to Arguments

Applicant's arguments filed 10/11/2005 have been fully considered but they are not persuasive.

- Applicant asserts that, gas microbubbles are formed by introducing a gas into water, a buffer, or blood without surfactant.

In response to this argument, it is the position of the examiner to confirm that since a surfactant is often an integral part of a gas microbubble, as shown by both Rasor and Schneider, the term "microbubble" cannot be used to exclude surfactant. Therefore, the term "a gas microbubble formed by a introducing a gas into...." does not exclude surfactant, as asserted. Further, the support for the amendment cited by the applicant demonstrates clearly that when dry relatively hydrophobic microparticle from a gaseous environment is introduced into a liquid such as buffer, water or blood, the

Art Unit: 1618

particles carries with it some of the gas into the liquid, which indicates that introducing the gas in the liquid medium is associated with the microparticle, which in turn makes it unclear how this would exclude surfactant from either the microparticles or gas microbubble or just from gas microbubble, as appears to be amended. Further, note in columns 5-6 of Rasor, that the microbubble are formed by dispersion in water and therefore it is the microparticles which stabilize the gas bubbles of Rasor that contain the surfactant and not the gas microbubbles themselves. Rasor also discloses that his composition is administered intravenously (see abstract), which reads on the limitations amended in the claim.

- Applicant makes the same assertion for Schneider as made of Rasor above, that the instant claims exclude making the claimed stabilized microbubbles with a surfactant.

As stated above, the claims are not limited to exclusion of a surfactant in making the claimed microbubbles. This assertion appears to contradict the definition of gas microbubble as known in the art. Third, the assertion appears to contradict the actual invention, which uses a surfactant in the microparticles that stabilize the gas microbubbles. The term "consisting essentially of" in the preamble of the claim cannot be used to specifically exclude something from one component in a claim while allowing it in another (i.e., excluding from the gas microbubbles but not the microparticles that stabilize the microbubbles). Further, the surfactants used in Schneider are used in the liposomes which are used to stabilize the gas bubbles that do not contain surfactant, which is the same as is asserted is being claimed. It is noted some of the dependent claims are product-by process claims, which are examined as reading on the product.

Art Unit: 1618

Also, the process in these claims is open-ended which recite comprising in the listed steps. Schneider also discloses that his invention composition suitable for injection into the bloodstream and body cavities of living beings, comprising a suspension of stabilized air or gas microbubbles in a physiologically acceptable aqueous carrier (claim 1), this aqueous carrier may be water, buffer, or blood,

- Applicant asserts that Rasor and Schneider use a surfactant in their microbubble compositions which is excluded from the claimed compositions and that Unger fails to remedy this deficiency.

This is not found persuasive because, for the reasons set forth above under the 102 rejections, Rasor and Schneider. The instant claims do not exclude the use of a surfactant. Further, Unger is relied on for teaching the use of ultrasound to rupture particles for releasing drug.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

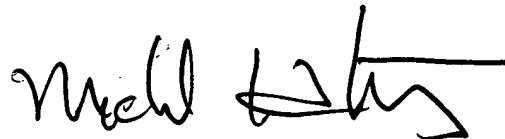
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1618

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nabila Ebrahim

2/24/06

A handwritten signature in black ink, appearing to read "Michael Hartley", with a stylized flourish at the end.

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER